

What is claimed is:

1. An isolated nucleic acid molecule encoding an inward rectifier, G-protein activated, mammalian, potassium KGA channel.
2. An isolated RNA molecule of claim 1.
3. An isolated DNA molecule of claim 1.
4. An isolated cDNA molecule of claim 3.
5. A plasmid comprising the molecule of claim 1.
6. The plasmid of claim 5, designated pBSIIKS(-)KGA (ATCC Accession No. 75469).
7. A nucleic acid molecule of at least 15 nucleotides capable of specifically hybridizing with the nucleic acid molecule of claim 1.
8. An isolated nucleic acid molecule of claim 1, operatively linked to a promoter of RNA transcription.
9. A vector comprising the nucleic acid molecule of claim 8.
10. A host vector system for the production of a polypeptide having the biological activity of a KGA channel which comprises the vector of claim 9 in a suitable host.
11. A host vector system of claim 10, wherein the suitable host is a bacterial cell, an insect cell, a mammalian cell, or a *Xenopus* oocyte.

12. A method for producing a polypeptide having the biological activity of a KGA channel which comprises culturing the host ~~vector~~ system of claim 10 under conditions permitting production of the polypeptide and recovering the polypeptide so produced.

13. A method for isolating from a sample a nucleic acid molecule encoding an inward rectifier, G-protein activated, potassium channel which comprises:

- (a) isolating nucleic acids from the sample;
- (b) contacting the isolated nucleic acids with the molecule of claim 7, under conditions permitting formation of a complex between the nucleic acid molecule encoding an inward rectifier, G-protein activated, potassium channel and the molecule of claim 7;
- (c) isolating the complex so formed; and
- (d) separating the nucleic acid molecule encoding an inward rectifier, G-protein activated, potassium channel from the complex, thereby isolating the nucleic acid molecule encoding an inward rectifier, G-protein activated, potassium channel.

14. A method for isolating DNA encoding an inward rectifier, G-protein activated, potassium channel or a fragment thereof in a sample which comprises:

- (a) isolating DNA from the sample;
- (b) denaturing the isolated DNA;

- 5 (c) reannealing the denatured DNA in the presence
of two unique single stranded nucleic acid
molecules of claim 7 that are complementary to
nucleotide sequences on opposite strands of
the DNA molecule encoding an inward rectifier,
G-protein activated, mammalian, potassium KGA
channel;
- 10 (d) polymerizing the reannealed nucleic acids with
DNA polymerase under conditions that allow DNA
polymerization;
- (e) denaturing the polymerized DNA of step (d);
- 15 (f) repeating steps (c) through (e) for 10 or more
cycles; and
- (g) isolating the polymerized DNA obtained from
step (f), thereby isolating DNA encoding an
inward rectifier, G-protein activated,
20 potassium channel or a fragment thereof.

25 15. A method for isolating DNA encoding an inward
rectifier, G-protein activated, potassium channel or a
fragment thereof in a sample which comprises:

- (a) isolating DNA from the sample;
- (b) denaturing the isolated DNA;
- 30 (c) reannealing the denatured DNA in the presence
of a unique single stranded nucleic acid
molecule of claim 7 and a nucleic acid
molecule encoding a known genomic repeat
35 sequence;

(d) polymerizing the reannealed nucleic acids with DNA polymerase under conditions that allow DNA polymerization;

(e) denaturing the polymerized DNA of step (d); and

(f) repeating steps (c) through (e) for 10 or more cycles; and

(g) isolating the polymerized DNA from step (f), thereby isolating DNA encoding an inward rectifier, G-protein activated, potassium channel or a fragment thereof.

16. A method of claim 13, wherein the molecule of claim 7 is labelled with a detectable marker.

17. A nucleic acid molecule isolated by the method of claim 13.

18. A purified inward rectifier, G-protein activated, mammalian, potassium KGA channel.

19. A purified channel of claim 18, having substantially the same amino acid sequence as the amino acid sequence shown in Figure 5.

20. A protein encoded by the isolated nucleic acid molecule of claim 1.

21. A method for determining whether an agent activates a KGA channel which comprises:

(a) contacting the host vector system of claim 10

with the agent under conditions permitting KGA channel conductance to be affected by known ion channel agonists or intracellular second messenger agonists; and

(b) detecting any change in KGA channel conductance, an increase in KGA channel conductance indicating that the agent activates the KGA channel.

22. An agent identified by the method of claim 21.

23. A pharmaceutical composition comprising an amount of the agent of claim 22, effective to increase KGA conductance and a pharmaceutical acceptable carrier.

24. A method for determining whether an agent deactivates a KGA channel which comprises:

(a) contacting the host vector system of claim 10 with the agent under conditions permitting KGA channel conductance to be affected by known ion channel antagonists or intracellular second messenger system agonist; and

(b) detecting any change in KGA channel conductance, a decrease in KGA channel conductance indicating that the agent deactivates the KGA channel.

25. An agent identified by the method of claim 24.

26. A pharmaceutical composition comprising an amount of the agent of claim 25, effective to decrease KGA channel conductance and a pharmaceutical acceptable carrier.

27. A method for identifying in a nucleic acid sample a nucleic acid molecule encoding a G-protein associated receptor which activates the inward rectifier, G-protein activated, mammalian, KGA potassium channel which comprises:

- (a) introducing nucleic acid molecules of claim 1 and the nucleic acid sample to a *Xenopus* oocyte under conditions permitting expression of both the receptor and the channel;
- (b) contacting the oocyte of step (a) with a panel of known G-protein associated receptor activators; and
- (c) detecting any change in KGA channel conductance, an increase in KGA channel conductance indicating the identification of a nucleic acid molecule encoding a G-protein associated receptor which activates the inward rectifier, G-protein activated, mammalian, KGA potassium channel.

28. A method for isolating from a cDNA expression library a cDNA clone encoding a G-protein associated receptor which activates the inward rectifier, G-protein activated, mammalian potassium KGA channel which comprises:

- (a) isolating cDNA from a sample containing a number of cDNA clones from the cDNA expression library;
- (b) transcribing the isolated cDNA to produce RNA;

- (c) isolating the RNA from the transcribed cDNA;
- (e) introducing the isolated RNA and together with nucleic acid molecules of claim 1 into a *Xenopus* oocyte under conditions permitting expression of the KGA channel and G-protein associated receptor;
- (f) contacting the oocyte of step (e) with a panel of known G-protein associated receptor activators;
- (g) detecting an increase in KGA channel conductance; and
- (h) repeating steps (a) through (g) using fewer cDNA clones from the sample until isolation of a single cDNA clone encoding a G-protein associated receptor which activates the KGA channel.

29. The cDNA clone isolated in claim 28.

30. The G-protein associated receptor encoded by the cDNA clone of claim 29.

31. A method for testing whether a G-protein associated receptor activates the inward rectifier, G-protein activated, mammalian, KGA potassium channel which comprises:

- (a) introducing a nucleic acid molecule of claim 1 and a nucleic acid molecule encoding the G-protein associated receptor to a *Xenopus* oocyte under conditions permitting expression

of both the receptor and the channel;

(b) contacting the oocyte of step (a) with a known G-protein associated receptor activator; and

(c) detecting any change in KGA channel conductance, an increase in KGA channel conductance indicating that the G-protein associated receptor activates the KGA channel.

32. A method for identifying in a nucleic acid sample a nucleic acid molecule encoding G-protein associated receptor capable of deactivating the inward rectifier, G-protein activated, mammalian KGA potassium channel comprising:

(a) introducing a nucleic acid molecule of claim 1, a nucleic acid molecule encoding a G-protein associated receptor known to activate the KGA channel, and the nucleic acid sample to a *Xenopus* oocyte under conditions permitting expression of the G-protein associated receptor known to activate the KGA channel, the KGA channel and a known G-protein associated receptor;

(b) contacting the oocyte of step (a) with a known G-protein associated receptor activator and a panel of known inhibitory G-protein associated receptor activators; and

(c) detecting any change in KGA channel conductance, a decrease in KGA channel conductance indicating the identification of a nucleic acid molecule encoding an inhibitory

G-protein associated receptor capable of deactivating the KGA channel in the sample.

33. A method for isolating from a cDNA expression library a cDNA clone encoding a G-protein associated receptor which deactivates the inward rectifier, G-protein activated, mammalian potassium KGA channel which comprises:

- (a) isolating cDNA from a sample containing a number of cDNA clones from the cDNA expression library;
- (b) transcribing the isolated cDNA to produce RNA;
- (c) isolating the RNA from the transcribed cDNA;
- (e) introducing the isolated RNA, a nucleic acid molecule encoding a known G-protein associated receptor which activates the KGA channel, and the nucleic acid molecule of claim 1 into a *Xenopus* oocyte under conditions permitting expression of the KGA channel and both receptors;
- (f) contacting the oocyte of step (e) with a panel of known G-protein associated receptor activators;
- (g) detecting a decrease in KGA channel conductance; and
- (h) repeating steps (a) through (g) using fewer cDNA clones from the sample until isolation of a single cDNA clone encoding a G-protein

associated receptor which activates the KGA channel.

34. The cDNA clone encoding the G-protein associated receptor of which deactivates the inward rectifier, G-protein associated, mammalian, potassium KGA channel of claim 33.

35. The G-protein associated receptor which deactivates the inward rectifier, G-protein associated, mammalian, potassium KGA channel encoded by the cDNA clone of claim 34.

36. A method for identifying a nucleic acid molecule encoding a G-protein associated receptor capable of deactivating the inward rectifier, G-protein activated, mammalian KGA potassium channel comprising:

(a) introducing the nucleic acid molecule of claim 1, a nucleic acid molecule encoding a G-protein associated receptor known to activate the KGA channel, and nucleic acid molecules encoding an G-protein associated receptor to a *Xenopus* oocyte under conditions permitting expression of both the receptors and the channel;

(b) contacting the oocyte of step (b) with a known activator for the G-protein associated receptor which activates the KGA channel and a known activator for the other G-protein associated receptor; and

(c) detecting any change in KGA channel conductance, a decrease in KGA channel

conductance indicating the identification of a nucleic acid molecule encoding the G-protein associated receptor capable of deactivating the KGA channel.

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37. An antibody directed against the channel of claim 18.

38. A monoclonal antibody of claim 37. ,

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